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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/583,738	05/31/2000	Hossein A. Ghanbari	018792/0180	2794

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EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/583,738	Applicant(s) GHANBARI ET AL.	
	Examiner Ginny Portner	Art Unit 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 29 November 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on 29 November 2004. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☒ They raise the issue of new matter (see NOTE below);
(c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See. (See 37 CFR 1.116 and 41.33(a)). attachment.

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☒ Newly proposed or amended claim(s) 31,32,45,46 and 51-58 would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none

Claim(s) objected to: 31,32,45,46 and 51-58.

Claim(s) rejected: 23-30,33,35-44,47,49 and 50.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment.

12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____

13. ☐ Other: _____.

Allowable Subject Matter

1. If claims 31-32, 45-46 and 51-58 were submitted in independent form, would define over the prior art of record.

2. For at least the following reason, the Amendment submitted November 29, 2004 has not been entered:

Claim 37 is proposed to be amended to recite the phrase “an each bacteriophage strain is effective in killing bacteria from at least 50% of bacterial isolates”.

a. This phrase defines a functionality not previously recited in the claimed method of treating a mammal suffering from bacterial infection.

b. Additionally, the term “bacterial isolates” raises a new issue, as it lacks antecedent basis in the claim, and recites the plural tense of “isolates” while the bacteriophage strains of this claim are “selected against one of the group consisting of”, rather than a plurality of isolates as newly proposed.

c. The newly proposed claim limitations seeks to require the bacteriophage to kill 50% of all of the bacterial isolates set forth in the recited Markush Group, which raises the issue of New Matter After Final, as the instant Specification does not disclose a bacteriophage strain that will kill 50% of all 21 genera recited in claim 37. Original descriptive support for a bacteriophage strain with the recited functionality against all of the recited genera of bacteria is not set forth in the instant Specification.

d. Additionally, claim 23, for which Applicant sites to show this combination of claim limitations has been search previously, it is the position of the examiner that

paragraph (3) of claim 23 is not the same combination of claim limitations proposed for amending claim 37.

- i. The proposed amendment is far broader than the claim limitations set forth in claim 23 which recites: “(3) each bacteriophage strain is effective in killing, in vitro, bacteria from at least about 50% of bacterial isolates, wherein the isolates are from the same strain of bacterial organism as that from which the bacteriophage strain is isolated;”
- ii. The method of claim 37 is in vivo method and the claim limitations of claim 23(3) are directed to an in vitro assay.
- iii. The proposed claim limitations for claim 37 do not require the “bacterial isolates” to be the “same strain of bacterial organism as that from which the bacteriophage strain is isolated as required by claim 23(3)), but refer to all of the members of the Markush group .

The proposed combination of claim limitations set forth in claim 37 clearly defines a different scope of invention than that recited in claim 23.

Response to Remarks

1. Applicant's Remarks filed November 29, 2004 have been fully considered but they are not persuasive.
2. The rejection of claims 23-25, 33, 37-39 and 47 under 35 U.S.C. 102(b) as being anticipated by Norris (US Pat. 4,957,686) is traversed on the grounds that :
 - a. Norris does not teach or suggest a bacteriophage capable of infecting more than one strain of *S.sanguis*

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- b. Norris does not indicate that the bacteriophage of Norris has a wide host range;
 - c. Norris does not teach serial isolation of phage preparations, by which the virulence of a phage can be dramatically increased.
3. It is the position of the examiner that the paragraph(1) from claim 23 requires the bacteriophage to be “selected against one of the group” and not the entire Markush group as suggested in Applicant’s traversal.
4. Norris does teach or suggest a preparation of bacteriophages that is a mixture of more than one bacteriophage (see Norris, col. 1, lines 48-49; col. 2, lines 1-5; col. 3, lines 46-53 and claim 3). Mixtures of bacteriophage would contain two or more strains of bacteriophage as recited in Applicant’s claimed methods. The word “mixture” and the phrase “at least one” includes a plurality of bacteriophage strains able to destroy disease causing bacteria.
5. The bacteriophage strains of Norris are capable of infecting more than one strain of bacteria. The guidance and teaching is through incorporation by reference to US Pat. 4,891,210 (see ‘686, col. 1, lines 44-52; col. 2, lines 1-11; col. 3, lines 42-45), as well as utilization of bacteriophage strains known in the art and deposited with the American Type Culture Collection (ATCC)(see ‘686, column 1, lines 56-57). Upon consideration of ‘210, at col. 2, bacteriophages are taught to provided “extended protection against acid production by *L.acidophilis* or similar strains”, thus teaching the bacteriophage to infect not only *L.acidophilis* but other strains as well. Additionally the examiner consulted the ATCC website for bacteriophages for *Streptococcus*, at the time Norris was filed, and found a deposited strain of bacteriophage which are specific for a group of *Streptococcus*, which would infect a plurality of strains and species of bacteria.
6. With respect to wide host range, Norris claims a method of administering a preparation of bacteriophage that are specific for bacteria that produce a substance for “adhering to the salivary pellicle” which covers a broad host range of bacteria that would include *S.mutans*, *S.sanguis*, *Lactobacilli*, *Actinomyes* and various anaerobic bacteria (see ‘686, col. 3, lines 1-3 and col. 4, claim 1). With respect to a single bacteriophage being able to infect a plurality of strains or species of bacteria, ATCC teaches known bacteriophage species that will infect *Streptococcus* group C bacteria, this group includes a plurality of strains and species of

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Streptococcus (ATCC number 21597-B1), in addition to other bacterial species (ATCC deposits of bacteriophage are attached herewith).

7. With respect Norris teaching a method of serial isolation of phage preparations, by which the virulence of a phage can be dramatically increased, it is the position of the examiner that the claimed invention is not directed to a method of increasing the virulence of bacteriophages, but to treating infection with a preparation of bacteriophage, the claimed methods not reciting preparations produced by a process that encompasses serial isolation. Applicant's arguments are not commensurate in scope with the instantly claimed methods steps. Norris '686, does disclose the propagation of phages in immense numbers, a process that is both practical and inexpensive (see '686, col. 1, lines 59-60). US Pat. 4,891,210 is incorporated by reference and discloses a method which includes propagating bacteriophages in cultures of host organism in liquid cultures (see '210, lines 3-7).

Applicant has not structurally distinguished the administered compositions from the administered compositions of Norris '686; Norris '686 inherently anticipates the instantly claimed invention.

8. The rejection of claims 23-24, 27, 29, 33, 37-38, 41, 43,47 under 35 U.S.C. 102(b) as being anticipated by Unilever (EP 0414304 A2), is traversed on the grounds that:

d. Unilever does not "teach Applicant's claimed purified, virulent, non-toxic, host specific bacteriophage preparations having a wide host range.";

e. Unilever is asserted to not teach serial isolation of phage preparations.

9. With respect to Applicant's assertion that the bacteriophage preparations of Unilever are not :

f. purified, the examiner would like to point to column 5, section "2.", which teaches the growth and purification of bacteriophages and column 4, lines 14-25, in which the bacteriophages are incorporated into toothpaste and mouth wash, and therefore must be isolated and purified compositions.

g. Virulent, see Unilever col. 2, lines 41-55, where the bacteriophages are disclosed to be capable of lysing one or more undesirable bacteria, and are therefore virulent to bacteria.

- h. Non-toxic, see Unilever, col. 7, claim 3 “hygiene purposes”, would include compositions that are non-toxic to skin (see claim 8, col. 7) and to the gums of the mouth (see claim 11) and for therapy (see claim 13).
 - i. Host specific, broad host range bacteriophages (see col. 2, lines 52-54 “infecting and lysing various types of bacteria”, defines a broad host range bacteriophage, that is specific to bacterial host cells (see col. 1, lines 1-6).
10. It is the position of the examiner that none of the claims require the administration of bacteriophage preparations that were obtained from a serial isolation process; Applicant’s arguments are not commensurate in scope with the instantly claimed method of treating a mammal. Even so, Unilever teaches a method of growing bacteriophages that includes at least first and second inoculations (see col. 5, lines 30-41 “again to re-inoculate more seeded broths and the procedure was repeated until a titer of more than 10^{10} /ml was obtained.”) The reference inherently anticipates the instantly claimed invention.
11. The rejection of claims 23-24,27,29,33,37-38,41,43,47 under 35 U.S.C. 102(b) as being anticipated by Day et al (EP 0403292, 1990), is traversed on the grounds that:
- j. Day et al does not “teach Applicant’s claimed purified, virulent, non-toxic, host specific bacteriophage preparations having a wide host range.”;
 - k. Day et al is asserted to not teach serial isolation of phage preparations; and
 - l. Day et al’s examples are asserted to only show the isolation of bacteriophages that infect only a single bacteria.
12. With respect to Applicant’s assertion that the bacteriophage preparations of Day et al are not :
- m. purified, the examiner would like to point to page 5, lines 47-56, where the bacteriophage preparation is purified.
 - n. Virulent, see page 3, lines 50-52, “the use of lytic phages is generally preferred, as infection results in the rapid destruction of the target bacterium.”
 - o. Non-toxic, see page 3, lines 35-36 “no adverse effect on flavour” and page 3, line 38 “so the food-stuff remains completely unaffected by their presence”, and functions as

a “medicament (see page 3, line 8)”. “No danger to humans or animal being infected by the phage” (see page 3, lines 47-48).

p. Host specific, broad host range bacteriophages (see page 3, lines 45-49), “highly specific in the organisms they can infection, any one variety of phage will only infect one species of bacterium and frequently only selected strains of that species”, thus teaching the bacteriophages to be specific for a plurality of strains, and specific for a species.

Additionally the reference discloses bacteriophage preparations directed against “several different species of bacterium” defining a broad host range preparation (see page 4, lines 6-8), and “specific for more than one family of bacterium” (see page 4, lines 18-19.)

13. It is the position of the examiner that none of the claims require the administration of bacteriophage preparations that were obtained from a serial isolation process; Applicant’s arguments are not commensurate in scope with the instantly claimed method of treating a mammal. The reference inherently anticipates the instantly claimed invention.

14. The rejection of claims 23-30, 33, 35-44, 47, 49-50 under 35 U.S.C. 103(a) as being unpatentable over Day et al (GB 2253859) in view of Merrill (US Pat 5,688,501), is traversed on the grounds that:

q. Day et al does not “teach Applicant’s claimed purified, virulent, non-toxic, host specific bacteriophage preparations having a wide host range.”;

r. Day et al is asserted to not teach serial isolation of phage preparations; and

s. Day et al’s examples are asserted to only show the isolation of bacteriophages that infect only a single bacteria.

15. It is the position of the examiner that Day et al teach the bacteriophage preparations to be:

t. purified, the examiner would like to point to page 7, paragraph 3, where the bacteriophage preparation is purified “ultracentrifugation and ultrafiltration”.

u. Virulent, see page 5, paragraph 4, “the use of lytic phages is generally preferred, as infection results in the rapid destruction.”

v. Non-toxic, see page 5, paragraph 2 “tasteless and harmless”, “no danger to the consumer of being infected by the phage” (see page 4, paragraph 7).

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w. Host specific, broad host range bacteriophages (see page 4, paragraph 6), highly specific in the organisms they can infect, any one variety of phage will only infect one species of bacterium and frequently only selected strains of that species”, thus teaching the bacteriophages to be specific for a plurality of strains, and specific for a species.

Additionally the reference discloses bacteriophage preparations directed against “several different species of bacterium” defining a broad host range preparation (see page 6, paragraph 4), and “specific for more than one family of bacterium” (see page 8, paragraph 2).

16. It is the position of the examiner that none of the claims require the administration of bacteriophage preparations that were obtained from a serial isolation process; Applicant’s arguments are not commensurate in scope with the instantly claimed method of treating a mammal. The reference inherently anticipates the instantly claimed invention.

17. Applicant further traverses the application of the combination of Day in view of Merrill et al because Day does not teach a combination composition that contains antibiotics and additional bacteriophages for species of bacterial pathogens recited in the claims.

18. It is the position of the examiner that Day et al was not applied against the claims under 35 USC 102, but 35 USC 103. Both Day et al and Merrill et al are directed to the formulation of bacteriophage preparations and the administration of the preparations to a mammal or animal (Day et al, see page 9, paragraphs 1-2; Merrill et al (all claims and entire document) and therefore are analogous art.

Day et al teaches that addition of other components to the bacteriophage preparation, to include carrier material, encapsulation material, and an additive product (see page 7, last paragraph, and page 8, first and second paragraphs). Therefore, Day et al teaches a combination of components added to the bacteriophage preparations to aid in the effectiveness of the bacteriophage preparation. Merrill et al teach bacteriophage preparations that contain a combination of components, one of which is an antibiotic, the antibiotic aiding in the bacteriophage preparation effectiveness against the target bacteria.

19. Merrill et al is traversed to not disclose virulent bacteriophages having a broad host range.

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20. It is the position of the examiner that Merrill et al was cited to show genus specific bacteriophages (see Merrill et al, claim 13) which would be specific for a plurality of species and strains of bacteria, thus defining bacteriophage preparations with a broad host range, and Merrill et al additionally teach the incorporation of antibiotics into a bacteriophage preparation to aid in the overall effectiveness of the bacteriophage preparation.

21. Merrill et al is traversed as not suggesting or teaching the combination of two or more bacteriophage strains.

22. It is the position of the examiner that Merrill et al was not applied against the claims under 35 USC 102, but under 35 USC 103, and Day et al was cited for teaching the combination of two or more bacteriophages against two or more bacteria (see discussion of Day). Merrill et al was applied against the claims in combination with Day et al, because Merrill et al teach clinically relevant bacteria for which bacteriophage preparations are available and are effective at the genus level for killing bacteria (Bacteriophages are available from Internationally recognized Bacteriophage Depositories (ATCC or WHO)) and Merrill et al also teach the combination of a bacteriophage preparation together with an antibiotic (see paper number 20, paragraph 2, incorporated herein by reference).

23. Applicant raises a question with respect to the full teaching set forth in Merrill et al with respect to what the scope of the phrase “adjunctive or stand alone (see col. 7, line 30)” therapy is; the examiner therefore, for clarity of the record, relied upon Day et al who specifically teach combination compositions of bacteriophages directed against different genera/species/strains of bacteria in combination with Merrill et al who Applicant agrees teaches the combination of bacteriophages with antibiotics, antimicrobial agents and chemotherapeutic agents. Day et al who teaches bacteriophage combination compositions directed against “several different species of bacterium (see Day et al, page 6, paragraph 6), such as bacteriophages specific for Clostridium together with Listeria was applied against the claims in view of Merrill et al because Merrill et al teach, suggest and provide guidance for the incorporation of antibiotics into bacteriophage preparations, and clearly points out clinically relevant bacteria for which bacteriophage therapy is needed. The claimed invention is obviated based on the combination of the teachings of Day

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et al in view of Merrill et al, for reasons of record in paper number 20, paragraph 13, and response to arguments set forth herein.

Conclusion

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
March 15, 2005

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ART UNIT 1645
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